Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	75	25
25	10	90
35	10	90
45	75	25
50	75	25

Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 220 nm
Column: 4.0-mm × 25-cm; packing L1
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Sample: *System suitability solution*
[NOTE—The relative retention times for losartan and triphenylmethanol are 1.0 and 1.9, respectively. The typical retention time for triphenylmethanol is 20 min.]
Suitability requirements
Tailing factor: NMT 1.6
Analysis
Sample: *Sample solution*
Calculate the percentage of each impurity in the portion of losartan potassium ($C_{22}H_{22}ClKN_6O$) taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response for each impurity
r_T = sum of the responses for all peaks
Acceptance criteria
Individual impurities: NMT 0.2%
Total impurities: NMT 0.5%

SPECIFIC TESTS

Change to read:

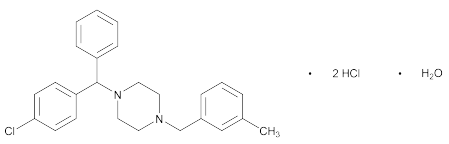
• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 0.5%. •If labeled as an amorphous form, NMT 5.0%.• (RB 1-Jan-2012)

ADDITIONAL REQUIREMENTS

Add the following:

•• **LABELING:** Where it is an amorphous form, the label so indicates.• (RB 1-Jan-2012)
• **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at controlled room temperature.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Losartan Potassium RS

Meclizine Hydrochloride



$C_{25}H_{27}ClN_2 \cdot 2HCl \cdot H_2O$ 481.88
$C_{25}H_{27}ClN_2 \cdot 2HCl$ 463.88

Piperazine, 1-[(4-chlorophenyl)phenylmethyl]-4-[(3-methylphenyl)methyl]-, dihydrochloride, monohydrate; 1-(*p*-Chloro-α-phenylbenzyl)-4-(*m*-methylbenzyl)piperazine dihydrochloride monohydrate [31884-77-2].
Anhydrous [1104-22-9].

DEFINITION

Change to read:

Meclizine Hydrochloride contains NLT 97.0% and ■NMT 102.0%■2S (*USP35*) of $C_{25}H_{27}ClN_2 \cdot 2HCl$, calculated on the anhydrous basis.

IDENTIFICATION

• **A. INFRARED ABSORPTION** ⟨**197K**⟩

Delete the following:

■• **B. ULTRAVIOLET ABSORPTION** ⟨**197U**⟩
Sample solution: 10 µg/mL in dilute hydrochloric acid (1 in 100)
Acceptance criteria: Meets the requirements■2S (*USP35*)

Change to read:

• ■**B.**■2S (*USP35*) **IDENTIFICATION TESTS—GENERAL,** *Choride* ⟨**191**⟩
Sample solution: Dissolve 25 mg in a mixture of 3 mL of 2 N nitric acid and 5 mL of alcohol.
Acceptance criteria: Meets the requirements

ASSAY

Change to read:

• **PROCEDURE**
■**Mobile phase:** Dissolve 1.5 g of sodium 1-heptanesulfonate in 300 mL of water, and mix this solution with 700 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 4.
Standard solution: 0.1 mg/mL of USP Meclizine Hydrochloride RS in *Mobile phase*
Sample solution: 0.1 mg/mL of Meclizine Hydrochloride in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 230 nm
Column: 4.6-mm × 25-cm; 5-µm packing L1
Flow rate: 1.3 mL/min
Injection size: 20 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 1.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of meclizine hydrochloride ($C_{25}H_{27}ClN_2 \cdot 2HCl$) in the portion of Meclizine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of meclizine from the *Sample solution*
r_S = peak response of meclizine from the *Standard solution*
C_S = concentration of USP Meclizine Hydrochloride RS in the *Standard solution* (mg/mL)
C_U = concentration of Meclizine Hydrochloride in the *Sample solution* (mg/mL)■2S (*USP35*)
Acceptance criteria: 97.0%–■102.0%■2S (*USP35*) on the anhydrous basis

IMPURITIES

• **RESIDUE ON IGNITION ⟨281⟩:** NMT 0.1%

Change to read:

• **ORGANIC IMPURITIES, ■PROCEDURE 1**

[NOTE—On the basis of the synthetic route, perform either *Procedure 1* or *Procedure 2*. *Procedure 2* is recommended when the isomeclizine impurity may be present.]■2S (*USP35*)

Mobile phase: Dissolve 1.5 g of sodium 1-heptanesulfonate in 300 mL of water, and mix this solution with 700 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 4.

System suitability solution: 0.01 mg/mL each of USP Meclizine Hydrochloride RS and 4-chlorobenzophenone in *Mobile phase*

Standard solution: 2.5 µg/mL of USP Meclizine Hydrochloride RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Meclizine Hydrochloride in *Mobile phase*

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Flow rate: 1.3 mL/min

Injection size: 20 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

[NOTE—The elution order is meclizine, followed by 4-chlorobenzophenone.]

Suitability requirements

Resolution: NLT 2.0 between meclizine hydrochloride and 4-chlorobenzophenone, *System suitability solution*

Column efficiency: NLT 1800 theoretical plates, determined from the analyte peak, *Standard solution*

Tailing factor: NMT 1.5 for the analyte peak, *Standard solution*

Relative standard deviation: NMT 1.5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Allow the *Sample solution* to elute for NLT three times the retention time of meclizine hydrochloride.

Calculate the percentage of each impurity in the portion of Meclizine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of meclizine from the *Standard solution*

C_S = concentration of USP Meclizine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Meclizine Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor, 0.72 for the 4-chlorobenzophenone peak and 1.0 for all other peaks

Acceptance criteria

Any individual impurity: NMT 0.5%

Total impurities: NMT 1.0%

Add the following:

■• **ORGANIC IMPURITIES, PROCEDURE 2**

Mobile phase: Dissolve 5 g of sodium 1-heptanesulfonate in 1000 mL of water, and mix 600 mL of this solution with 400 mL of acetonitrile. Adjust with 0.1 N sulfuric acid to a pH of 4.0 ± 0.1.

System suitability solution: 2.5 µg/mL each of USP Meclizine Hydrochloride RS, USP Meclizine Related Compound A RS, and USP Meclizine Related Compound B RS in *Mobile phase*

Standard solution: 2.5 µg/mL of USP Meclizine Hydrochloride RS in *Mobile phase*

Sample solution: 0.5 mg/mL of Meclizine Hydrochloride in *Mobile phase*. [NOTE—Store this solution no longer than 24 h.]

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 210 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 50°

Flow rate: 2.0 mL/min

Injection size: 30 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between meclizine related compound B and meclizine, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 6.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each impurity in the portion of Meclizine Hydrochloride taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of meclizine from the *Standard solution*

C_S = concentration of USP Meclizine Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = concentration of Meclizine Hydrochloride in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 1*)

Acceptance criteria: See *Table 1*. Disregard any peak eluting before 1.75 min.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
3-Methylbenzyl alcohol	0.11	1.0	0.10
1,4-Bis(3-methylbenzyl) piperazine	0.22	0.73	0.10
4-Chlorobenzhydrol[a]	0.53	1.3	0.15
Meclizine *o*-chloro isomer[b]	0.81	1.0	0.10
Isomeclizine (meclizine *o*-methyl isomer)[c]	0.90	1.1	0.15
Meclizine	1.0	—	—
Any individual unspecified impurity	—	1.0	0.10
Total impurities	—	—	1.0

[a] USP Meclizine Related Compound A.

[b] 1-[2-Chlorophenyl)(phenyl)methyl]-4-(3-methylbenzyl) piperazine.

[c] USP Meclizine Related Compound B.

■2S (*USP35*)

SPECIFIC TESTS
• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 5.0%

ADDITIONAL REQUIREMENTS

Change to read:

• **PACKAGING AND STORAGE:** Preserve in tight containers. ■Store at room temperature.■2S *(USP35)*

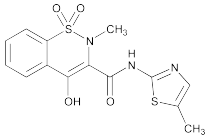
Add the following:

■• **LABELING:** If a test for *Organic Impurities* other than *Procedure 1* is used, the labeling states the test with which the article complies.■2S *(USP35)*

Change to read:

• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Meclizine Hydrochloride RS
■USP Meclizine Related Compound A RS
4-Chlorobenzhydrol.
$C_{13}H_{11}ClO$ 218.68
USP Meclizine Related Compound B RS
Isomeclizine
1-[(4-Chlorophenyl)(phenyl)methyl]-4-(2-methylbenzyl)piperazine dihydrochloride monohydrate.
$C_{25}H_{27}ClN_2 \cdot 2HCl \cdot H_2O$ 481.88■2S *(USP35)*

Meloxicam



$C_{14}H_{13}N_3O_4S_2$ 351.40
4-Hydroxy-2-methyl-*N*-(5-methyl-2-thiazolyl)-2*H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide [71125-38-7].

DEFINITION
Meloxicam contains NLT 99.0% and NMT 100.5% of meloxicam ($C_{14}H_{13}N_3O_4S_2$), calculated on the dried basis.

IDENTIFICATION
• **A. INFRARED ABSORPTION** ⟨**197K**⟩
• **B. ULTRAVIOLET ABSORPTION** ⟨**197U**⟩
Wavelength range: 240–450 nm
Sample solution: 10 µg/mL in methanol

ASSAY
• **PROCEDURE**
Solution A: Mixture of a 0.1% (w/v) solution of ammonium acetate adjusted with 10% ammonia solution to a pH of 9.1
Mobile phase: Methanol and *Solution A* (21:29)
Diluent: Methanol and 1 N sodium hydroxide (250:1)
System suitability solution: 0.08 mg/mL each of USP Meloxicam RS and USP Meloxicam Related Compound A RS. Prepared by dissolving in 50% of the flask volume of *Diluent* and diluting with water to volume.
Standard solution: 0.2 mg/mL of USP Meloxicam RS. Prepared by dissolving in 50% of the flask volume of *Diluent* and diluting with water to volume.
Sample solution: 0.2 mg/mL of Meloxicam. Prepared by dissolving in 50% of the flask volume of *Diluent* and diluting with water to volume.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)
Mode: LC
Detector: UV 360 nm
Column: 4.6-mm × 15-cm; packing L1
Column temperature: 45°
Flow rate: 1 mL/min
Injection volume: 10 µL
System suitability
Sample: *System suitability solution*
[NOTE—The relative retention times for meloxicam related compound A and meloxicam are 0.7 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 3.0 between meloxicam related compound A and meloxicam
Tailing factor: NMT 2.0 for the meloxicam peak
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of meloxicam ($C_{14}H_{13}N_3O_4S_2$) in the portion of Meloxicam taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of meloxicam from the *Sample solution*
r_S = peak response of meloxicam from the *Standard solution*
C_S = concentration of USP Meloxicam RS in the *Standard solution* (mg/mL)
C_U = concentration of the *Sample solution* (mg/mL)
Acceptance criteria: 99.0%–100.5% on the dried basis

IMPURITIES
• **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
• **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm
• **ORGANIC IMPURITIES, PROCEDURE 1**
Perform either *Procedure 1* or *Procedure 2*, depending on the manufacturing process used.
Solution A: 0.1% (w/v) solution of monobasic potassium phosphate adjusted with 1 N sodium hydroxide to a pH of 6.0
Solution B: Methanol
Diluent: Methanol and 1 N sodium hydroxide (50:3)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	60	40
2	60	40
10	30	70
15	30	70
15.1	60	40
18	60	40

System suitability solution: 0.08 mg/mL each of USP Meloxicam RS, USP Meloxicam Related Compound A RS, and USP Meloxicam Related Compound B RS. Prepared by dissolving in 10% of the flask volume of *Diluent* and diluting with water to volume.
Standard stock solution: 0.6 mg/mL of USP Meloxicam RS. Prepared by dissolving in 25% of the flask volume of *Diluent* and diluting with methanol to volume.
Standard solution: 0.012 mg/mL of USP Meloxicam RS in methanol from the *Standard stock solution*
Sample solution: 4 mg/mL of Meloxicam. Prepared by dissolving in 25% of the flask volume of *Diluent* and diluting with methanol to volume.
Chromatographic system
(See *Chromatography* ⟨621⟩, *System Suitability*.)